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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,877	04/17/2002	Toshio Miyata	2605/102	5152

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EXAMINER
HANLEY, SUSAN MARIE

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,877	MIYATA, TOSHIO	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7, 10-12 and 14-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7, 9, 12 and 15 of copending Application No. 10/089,789. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '789 are directed to a carrier comprising one or more immobilized biguanidine agents and a method of using said carrier to remove carbonyl compounds. These inventions are species of the genus of the instant application which is directed to immobilized carbonyl-trapping compounds and a method of using said immobilized compounds to trap carbonyl compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20, 21, 27-39 of copending Application No. 09/763,286 Although the conflicting claims are not identical, they are not patentably distinct from each other because the method claimed by '286, which is directed to preparing a peritoneal dialysate, carries out the same steps as claims 15-16, which is directed to a method of improving the carbonyl stress state in blood in a hemodialysis circuit, of the instant application. Further, the execution of the claimed method of '286 requires or makes the carbonyl-trapping agents of the instant application .

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 10/168,695 Although the conflicting claims are not identical, they are not patentably distinct from each other because the carbonyl trapping agent of '695 and the method of hemodialysis using said agent is a specie of the carbonyl-trapping agent and method thereof of the instant application. '695 is drawn to a carbonyl-trapping agent comprising glyoxalase I and a carbonyl-trapping agent. The agent of the instant application comprises a carbonyl-trapping agent. The open language of the instant application allows for other components in the agent. Glyoxalase I is compatible with a carbonyl-trapping agent because it can remove carbonyl compounds by catalyzing bond formation between a carbonyl agent and a carbonyl compound. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "removes a blood carbonyl compound" in independent claim 1 is vague and indefinite because it is unclear from what or from where the carbonyl-trapping agent is removing blood.

Claims 10 and 11 are rejected because the term "active" is a relative term and no comparison is made.

Claim Rejections - 35 USC § 102

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6, 7 and 10-16 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Kurokawa et al. (WO 00/10606, reference AD in the IDS).

Kurolawa et al. disclose drugs for relieving carbonyl stress in peritoneal dialysates comprising carbonyl-trapping compounds such as aminoguanidine, as in claims 1-3, 7, 10 , 11, 14 and 15. Carbonyl compounds that are formed during sterilization and storage of peritoneal dialysates are eliminated by contacting them with the trapping agents. The trapping agents can also be attached to a cartridge thus enabling the elimination of carbonyl compounds during the dialysis circuit, as in claims 4, 12, 15 and 16 (abstract). Aminoguanidine is inherently a Maillard reaction inhibitor since it reacts with carbonyl groups, as in claims 6 and 13.

This is an intervening reference since the inventive entity differs from the authorship of the prior art. It can be overcome by the submission of a certified translation of the priority document.

Claims 1, 2, 6, 8-11 and 13 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Nakashima et al. (US 4,171,283).

Nakashima et al. disclose that hemodialysis has been accomplished with adsorbents such as activated carbon or anion exchange resin to remove toxins from blood (col. 1, lines 10-18). Although Nakashima et al. does not teach the carbonyl-trapping property or the ability of either agent to inhibit a Maillard reaction, such properties are inherent to the agents. The claiming of a new use, new functions or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1152, 1254, 195 USPO 430, 433 (CCPA 1977).

Claims 1-4, 6, 7 and 10-16 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Miyata et al. (Feb. 1999, reference EL in the IDS).

Miyata et al. disclose that carbonyl stress in uremia may contribute to long-term complications associated with chronic renal failure and dialysis. Carbonyl compounds such as glyoxal are responsible for reacting with carbohydrates and lipids to form advanced glycation products (abstract). Miyata et al. disclose that aminoguanidine and OPB-9195 (2-isopropylidenehydrazono-4-oxo-thiazolidin-5-ylacetanilide) inhibit AGE formation by reacting with carbonyl compounds responsible for AGE-formation, as in claims 1, 2, 7, 10-12, 15 and 16. Miyata et al. teach that AGE inhibitors could be immobilized in cartridges to extract reactive carbonyl compounds from blood during blood dialysis therapy, as in claims 3, 4 and 12 (p. 396, right column). The disclosed trapping agents are inherently Maillard reaction inhibitors since they react with carbonyl groups, as in claims 6 and 13.

Claims 1, 2, 6, 7, 10, 11, 13 and 14 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Miyata et al. (1998, reference EJ in the IDS).

Miyata et al. disclose that aminoguanidine and OPB-9195 (2-isopropylidenehydrazono-4-oxo-thiazolidin-5-ylacetanilide) inhibit AGE formation by reacting with carbonyl compounds in blood samples. Miyata et al. teach that 2,4-dinitrophenylhydrazine also reacts with carbonyl groups in blood, as in claims 1, 2, 7, 10, 11 and 14 (abstract). Hence, 2,4-dinitrophenylhydrazine, aminoguanidine and OPB-9195 are all carbonyl trapping agents that inhibit the Maillard, as in claims 6 and 13, reaction and AGE formation.

Claims 1-3, 6, 7, 10, 11, 13 and 14 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Lundstrom et al. (WO 96/02838).

Lundstrom et al. discloses that thiol agents such as glutathione, 3-mercaptopropionic acid and L-cysteine were immobilized on a polymer, silicon, glass or metal surface which are inherently insoluble in blood, as in claims 1-3, 7, 10, 11 and 14 (p. 4, lines 30-32). The immobilized thiol can be employed as a medical device especially for contact with blood. The disclosed invention meets the limitations of claims 1-3 because any of the thiols react with carbonyl compounds and are compatible with blood. The phrases "removes a blood carbonyl compound", "improves carbonyl stress state" are intended use and carries no patentable weight except that the prior art compound must be blood compatible. Chemical properties are inherent to a compound. Thiols are known to react with carbonyls and reducing sugars (a Maillard reaction), as in claims 6 and 13.

Hence, the disclosure by Lundstrom et al. clearly anticipates claims 1-3, 6, 7, 10, 11, 13 and 14 because the disclosed immobilized thiol compounds that react with carbonyls and reducing sugars.

Claims 1-4, 6, 7, 10, 11, 13, 14, rejected under 35 U.S.C. 102(e) as being anticipated by Haik, Jr. (US 6,727,285) in light of Ofsthun et al. (US 5,868,936).

Haik discloses a method of blocking toxic carbonyl and dicarbonyl compounds in blood by contacting the blood with an effective quantity of L- or D- arginine, or a modified arginine, as in claims 1, 2, 710 and 11. Claims 7 and 14 state that the trapping agent can be an aminoguanidine or a derivative thereof. According to Applicant definition of "derivative" (p.5), guanidine is a derivative of aminoguanidine because it has a substitution of a hydrogen atom at the corresponding position of the parent compound which has a methyl group. Hence, Haik meets the limitations of claims 7 and 14. Guanidine reacts with carbonyls and is an inherent Maillard reaction inhibitor, as in claims 6 and 13. Arginine reacts with carbonyls, such as glyoxal or methylglyoxal, and removes them from the blood supply. Haik teaches that the arginine can be administered to extracorporeal blood or blood products to scavenge carbonyl compounds. Haik discloses that the treated blood is filterable or can be left in the blood (col. 13, lines 10-20). Haik also teaches that that the disclosed method of removing carbonyl compounds from extracorporeal blood can be accomplished by any of the methods or apparatus taught by several patents. These references have been incorporated by reference and are therefore part of Haik's disclosure. For instance, Ofsthun et al. teach an improved bioaffinity membrane device for the removal of target molecules in blood for hemodialysis. A ligand is attached to the membrane fiber so that it can bind and/or react with the target in order to remove the target from the blood, as in claims 3, 4, 12, 15 and 16 (abstract, col. 16, lines 50-68). Thus, Haik discloses that the D- or L- arginine can be bound to a membrane filter to remove targets from blood for hemodialysis. The disclosure by Ofsthun et al. is a supporting reference and properly used in a rejection under of U.S.C. 102 since it was incorporated by reference in Haik to describe a method of using the invention of Haik in a dialysis membrane. MPEP 2131.01.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haik, Jr. (US 6,727,285) or Lundstrom et al. (WO 9602838) in view of Fishbane et al. (1997) and Ofsthun et al. (US 5,868,936).

The disclosures of Haik and Lundstrom et al. teach that carbonyl-trapping compounds can be immobilized on membranes for hemodialysis.

Neither Haik nor Lundstrom et al. teach that carbonyl-trapping compounds can be immobilized on polysulfone membranes.

Fishbane et al. disclose that high flux hemodialysis polysulfone membranes are more effective for the removal of circulating advanced glycation end-products (AGEs) during hemodialysis than low flux hemodialysis membranes and that enhanced removal of AGEs could significantly benefit the clinical outcome of diabetic patients with renal insufficiency (abstract).

Ofsthun et al. teach that affinity ligands can be immobilized on hollow fiber membranes for hemodialysis. The hollow fiber membrane should be made of a blood compatible material such as a polysulfone. A polysulfone material is only one of a number of apparently equal alternatives for materials that are suitable for hemodialysis (col. 7, lines 58068).

It would have obvious to one of ordinary skill in the art at the time the invention was made to immobilize the carbonyl-trapping compounds taught by Haik et al. or Lundstrom et al. to a polysulfone membrane for hemodialysis. The ordinary artisan would have been motivated to do so because polysulfone materials are well known for use in hemodialysis membranes and they have the advantage of being able to clear more AGEs than low flux membranes. This would be advantageous to a hemodialysis patient a polysulfone membrane having an immobilized carbonyl-trapping compound could clear the carbonyl compounds that are responsible for glycation as well as any AGEs already present in the blood. The ordinary artisan would have had a reasonable expectation that carbonyl-trapping compounds could be immobilized on a polysulfone membrane for hemodialysis because other affinity agents have been successfully attached to polysulfone membranes and then used for hemodialysis procedures.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEAN C. WITZ
PRIMARY EXAMINER